

**REMARKS****I. Elected Subject Matter**

In the Response to Restriction Requirement, filed June 3, 2002, the Applicants elected a polypeptide comprising at least residues 63-469 of SEQ ID NO: 2 as a molecular embodiment, selecting one of the species listed in paragraph 6A of the Action, as required by the Action. The more recent communication invited the Applicants to elect any molecular embodiment relating to SEQ ID NO: 2. In response, the Applicants wish to elect a polypeptide comprising at least residues 63-468. This elected fragment is consistent with the existing claims, in particular, claim 57 which is directed to a hu-Asp1 amino acid sequence lacking the amino acids 469-492.

In the Notice, the Examiner stated that the elected subject matter is inconsistent with the pending claims. As noted above, the Applicants elected a polypeptide comprising at least residues 63-468 of SEQ ID NO: 2. New claim 78 is specifically directed to this elected fragment and is supported at page 26, lines 12-18, and therefore does not add new matter to the application. Pending claims 53, 54, 55 and 56 are generic claims that read on the elected fragment. Claims 57, 58 and 59 are directed to specific fragments of SEQ ID NO: 2 that read on the elected fragment. Claims 60, 61, 62, 63, 64, 65, 66, 67 and 70 depend from claim 53 and are directed to a use of a generic form of the hu-Asp1 polypeptide and therefore also read on (use of) the elected fragment.

**II. Compliance with the Sequence Rules**

In the Communication, the Examiner also asserted that the present application is not in compliance with the Sequence Requirements, as indicated in the Office Action mailed January 4, 2002. In response, claim 62 has been amended to identify the recited amino acid sequences with a sequence identification number. The amino acid sequence LVFFAEDF was not recited in the sequence listing and therefore a third substitute sequence listing is submitted herewith. The amino acid sequence LVFFAEDF is defined as an  $\alpha$ -secretase cleavage site at page 26, lines 27-29. Accordingly, sequence identification numbers have also have been added at page 26 to define these recited  $\alpha$ -secretase cleavage sites. Thus, the substitute sequence listing and amendments do not add new matter to the application.

The Examiner also asserted that claim 57 encompasses a sequence that joins two non-contiguous segments and therefore does not comply with the Sequence Requirements set out in 37 C.F.R. § 1.822(o). The amino acid sequences recited in the claims do not require the joining of amino acids 1-468 and 493-518, and it is only required that the claimed amino acid sequence lack residues 469-492 of SEQ ID NO: 2. There is no requirement that residues 493-518 are retained. Therefore, the requirements of 37 C.F.R. § 1.822(o) does not apply herein. The Applicants believe they are in compliance with the current Sequence Requirements and request examination of the pending claims.

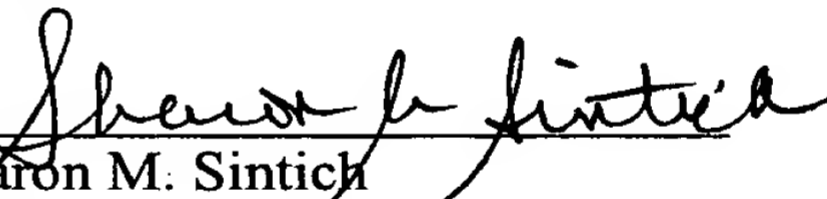
### CONCLUSION

Attached hereto is a marked-up version of the changes made to the specification and claims by the current amendment. The attached page is captioned "Version with markings to show changes made."

The Applicants believe pending claims 57-67, 70 and 78 are in condition for allowance and early notice thereof is requested.

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**VERSION WITH MARKINGS TO SHOW CHANGES MADE****IN THE SPECIFICATION**

The invention also encompasses methods of assaying for  $\alpha$ -secretase activity where hu-Asp1 protein and its substrate are brought into contact by a growing cell transfected or transformed with a polynucleotide encoding the hu-Asp1 protein or a fragment thereof that retains  $\alpha$ -secretase activity under conditions where the cell expresses hu-Asp1 protein in the presence of the APP substrate. The APP substrate in such circumstances can be exogenously introduced, or more preferably, is expressed by the cell that expresses Asp1. These methods also encompass contacting hu-Asp1 protein with a cell that expresses a polynucleotide that encodes an APP substrate containing an  $\alpha$ -secretase cleavage site. For example, the cell may express a polynucleotide that encodes a polypeptide having an  $\alpha$ -secretase cleavage site comprising the amino acid sequence LVFFAEDF (**SEQ ID NO: 84**) or KLVFFAED (**SEQ ID NO: 73**). In addition, the APP substrate may comprise any human isoform of APP, such as "normal" APP (APP695), APP 751, or APP770. These APP substrates can be further modified to comprise a carboxy-terminal di-lysine motif.

**IN THE CLAIMS**

62. (Amended) A method of claim 53, wherein the APP substrate  $\alpha$ -secretase cleavage site comprises the amino acid sequence LVFFAEDF (**SEQ ID NO: 84**) or KLVFFAED (**SEQ ID NO: 73**).